

phenotype of a transgenic mouse cannot be predicted.” (Office Action, page 2). Finally, both the Rule 132 Declaration and the references cited therein were deemed unpersuasive. (Office Action, page 5).

Because it is neither legally nor factually correct to assert that the phenotype of the claimed animals would be unpredictable or that sufficient identifying characteristics can never be present without actually making a transgenic animal, Applicants traverse the rejection and supporting remarks.

As previously noted, the guidelines on written description are clear -- the written description requirement is highly fact-dependent and there is a strong presumption that an adequate written description of the claimed invention is present at the time of filing. Further,

[t]he description need only describe in detail that which is new or not conventional. This is equally true whether the claimed invention is a product or a process. An applicant may also show that an invention is complete by disclosure of sufficiently detailed, relevant identifying characteristics which provide evidence that the applicant was in possession of the claimed invention, i.e. complete or partial structure, other physical and/or chemical properties, functional characteristics when coupled with known or disclosed correlation between function and structure, or some combination of such characteristics. (Final Examiner Guidelines on Written Description, 66 Fed. Reg. 1099, emphasis added).

Simply put, there is absolutely no requirement that Applicants actually make a transgenic mouse falling within the scope of the claims in order to adequately describe the animal’s phenotype. Rather, the test is whether there are sufficiently detailed, relevant identifying characteristics of the animals provided by Applicants to satisfy the written description requirement.

For the reasons of record and those presented herein, the specification as filed more than adequately describes and details relevant identifying characteristics of the animals of claims 38 and 65-68. Because the written description inquiry is highly fact-dependent, it is important to note at the outset of this discussion that the claimed transgenic mice are not used as disease models and, accordingly, do not exhibit a “traditional” transgenic animal phenotype. Moreover, unlike “traditional” transgenic animals, it is immaterial to the claimed invention where the transgenes integrate into the host’s genome. Instead, all that is required by the claims is that the mice are alive, that the claimed panel of expression cassettes are integrated somewhere in the animal’s

genome and that, under certain conditions, the mice are capable of generating and emitting detectable amounts of light. The specification as filed more than adequately describes such transgenic animals.

Simply put, the written description inquiry in this case does not hinge on the actually making the transgenic mouse and determining phenotype, but, rather, on whether the specification describes the characteristics of the panel of expression cassettes introduced into the animal, how these cassettes are introduced, how light is generated and how imaging is performed. For the reasons of record, the specification clearly describes all the relevant identifying characteristics of the claimed animals and, as such, the written description requirement of section 112 is satisfied.

The References Cited by the Office Do Not Establish Unpredictability

Turning now to the Examiner's contention that Wood, Cameron and Cui render the claimed transgenic animals "unpredictable," Applicants traverse the Examiner's premise and supporting remarks. (See, e.g., Office Action, paragraph bridging pages 2 and 3 for a discussion of Wood and previous Office Actions for discussions of Cameron and Cui).

As detailed above, the claimed animals are not used as traditional disease-models (e.g., as described in Wood) and, consequently, the phenotype of the claimed mice can in fact be determined *a priori*. Indeed, the claimed mice are useful simply by virtue of having integrated the claimed panel of expression cassettes into their genome (and thus being capable of emitting detectable amounts of light under certain conditions). In light of the fundamental differences between the claimed animals and the disease-model animals of Wood, it is clear that this reference establishes nothing regarding the state of the art or predictability of the particularly claimed animals and is utterly irrelevant to the instant written description inquiry.

Similarly, the claimed mice are entirely different from the transgenic animal technology described in Cameron and Cui. Again, the pending claims are directed to transgenic mice, while Cameron is focused on the lack of ES cells in livestock. For its part, Cui does not, by mere mention of luciferase, establish unpredictability of the claimed invention. Nearly six years prior to the effective filing date of the present specification, Cui identified the need for transgenic animals including reporter genes. In other words, Cui recognized and articulated a problem facing those working in this field and it was not until much later that the present inventors solved this problem (and,

indeed, solved it in a manner not suggested by Cui). Like Wood and Cameron, Cui does nothing to establish “unpredictability” of the precisely-claimed subject matter.

In sum, the references cited by the Examiner do not in any way establish that the inventors were not in possession of the claimed invention when the application was filed.

Additional Evidence of Record

Although not required, Applicants have provided still further evidence regarding the adequacy of the description of the claimed animals (or “the predictability of the phenotype” as phrased by the Examiner). This evidence, including patent and journal article references, demonstrates two key facts. First, transgenic mice containing a single expression cassette comprising a sequence encoding a light-generating protein have the predictable phenotype/identifying characteristic of emitting detectable amounts of light under certain conditions. (See, U.S. Patent No. 6,217,847). In view of the teachings and the specification (including reference to this patent), one of skill in the art would have known that Applicants were in possession of the claimed mice at the time of filing.

Second, the introduction of multiple expression cassettes is not, in and of itself, considered unpredictable. (See, Jankowsky, cited in previous Response). The Examiner has erred in dismissing Jankowsky as irrelevant on the grounds that it is a post-filing date reference. As an established expert in the field, Dr. West is entitled to rely on that evidence which was available to him at the time of filing. *See, e.g., In re Alton*, 37 USPQ2d 1578 (Fed. Cir. 1996). Although Jankowsky was published after the effective filing date, Dr. West properly uses this reference to illustrate his point that a skilled artisan would have known that introducing multiple expression cassettes was considered predictable at the time of filing. (See, West Declaration, paragraph 9). As discussed in detail below, the Office cannot ignore Dr. West’s opinions because they are based on factual underpinnings. Clearly, given the evidence of record, the phenotype of the specifically claimed animals is, in fact, quite predictable *a priori* based on the expression cassettes the mice contain.

Accordingly, the written description found in the specification regarding the expression cassettes, making transgenic mice comprising light-generating proteins and the like more than satisfies the written description requirement of 35 U.S.C. 112, first paragraph.

### 35 U.S.C. §112, First Paragraph, Enablement

The Examiner maintains that undue experimentation would be required in order to practice the invention of claims 38, 40, 41, 43, 45, 46, 49 and 65-68. As with written description, the Examiner asserts that both the transgenic mice comprising a panel of expression cassettes themselves and methods of determining the effect of an analyte using these mice would have required undue experimentation and was unpredictable. (e.g., Office Action, pages 7 and 8). As with written description, the Examiner's position is that, in any and all cases involving transgenic animals, the specification is not enabling if the mice were not actually made and their phenotype observed. *Id.* Cameron, Cui and Wood are cited as above for allegedly establishing unpredictability and the references cited by Applicants and Dr. West dismissed. Office Action, page 8.

By requiring actual production of the claimed animals, the Office has not applied the proper enablement standard. It is axiomatic that working examples are **never** required in order to show enablement. See, MPEP 2164.02. Furthermore, because the claimed animals are not used as disease-models, they are necessarily subject to a different enablement inquiry than traditional transgenic animals, particularly the traditional transgenic animals described in the references cited by the Examiner. Under the proper enablement standard, it is plain that the specification as filed makes it routine for the skilled worker to make and use the claimed mice and, moreover, to use these mice to determine the effect of an analyte.

Furthermore, even relatively out-dated Patent Office Training materials recognize that claims to transgenic animals are fully enabled where "an enabled use for the claimed transgenic mouse is well established." (See, Training Materials for Examining Patent Applications with Respect to 35 U.S.C. 112, first paragraph -- Enablement, Example I, page I-6, *circa* 1997). In the case at hand, an enabled use for transgenic animals comprising expression cassettes encoding a light-generating protein is well established, as evidenced for example by U.S. Patent No. 6,217,847 which shows the generation of a transgenic animal comprising an expression cassette encoding luciferase and use of these animals for the temporal and spatial analysis of transcriptional control. When the claims at hand are properly interpreted, there is absolutely no reason to doubt the predictability of making and using animals containing more than one such expression cassettes in light of the present disclosure.

For the reasons detailed above, Wood, Cameron and Cui are not germane to the claimed animals -- Wood because it addresses only on disease-model animals, Cameron

because is addresses only livestock and Cui because it merely identifies a problem (which Applicants then solved 6 years later).

The Examiner also errs in dismissing the Rule 132 Declaration and the Jankowsky reference. (See, also discussion of Declaration below). In this regard, the Examiner asserts Jankowsky is not relevant "since it is a post filing art published more than two years after the effective filing date of the claimed invention and since there is no evidence that Jankowsky et al. used the method disclosed in the specification." (Office Action, page 8). It is well settled that post-filing date references can be used to support enablement. *See, e.g., Gould v. Quigg* 3 USPQ2d 1302 (Fed. Cir. 1987). Like the post-filing date reference in *Gould*, Jankowsky was offered in the pending case not to supplement the disclosure but "as evidence of the level of ordinary skill in the art at the time of the application and as evidence that the disclosed [invention] would have been operative." *Id.* at 1305. Contrary to the Examiner's statement, Dr. West does indeed state that the methods used by Jankowsky and those described in the specification were both considered routine. In brief, Jankowsky is properly cited to establish that the skilled artisan could have readily made and used the claimed animals following the teachings of the specification (and references cited therein).

Thus, as the evidence of record makes clear, the teachings of the specification are more than sufficient to enable one of skill in the art to practice the claimed invention. Applicants respectfully request that the rejection of the claims under 35 U.S.C 112, first paragraph, be withdrawn.

#### **Declaratory Evidence Has Not Been Properly Considered**

The Examiner has erred in dismissing Dr. West's declaration as allegedly failing to "provide any evidence that would support the applicants arguments that they had possession of the claimed invention at the time of invention." (Office Action, page 5).

It is well established that declaratory evidence must be considered. In *In re Alton*, The Court of Appeals for the Federal Circuit held that it was error for the Examiner to dismiss, with conclusory statements, not only factual statements but also statements of opinion presented in Declarations made by qualified persons of ordinary skill in the art. The court commented that they were "aware of no reason why opinion evidence relating to a fact issue should not be considered by an Examiner." 37 USPQ2d 1578 at 1583 n10. Further, it is appropriate to consider extrinsic evidence to explain the disclosure of a reference. The role of extrinsic evidence is to educate the decision-maker to what the

reference meant to persons of ordinary skill in the field of the invention. *Scripps Clinic & Research Foundation v. Genentech, Inc.*, 18 USPQ2d 18996 (Fed. Cir. 1991).

Dr. West's declaration conclusively demonstrates that the specification adequately describes the claimed transgenic animals and that such animals were in the possession of the inventors at the time of filing and that undue experimentation would not be required to practice the invention as claimed. Dr. West also states, based on the facts presented in the references, that Cameron and Cui are not relevant to the claimed transgenic mice. The Office in the pending case has failed to adequately consider and rebut the facts and reasoned conclusions presented in the West Declaration regarding description and enablement. When properly considered, the Declaration of record in the application clearly establishes adequacy of disclosure, possession of the invention and enablement.

### CONCLUSION

Applicant respectfully submits that the claims comply with the requirements of 35 U.S.C. §112 and define an invention that is patentable over the art. Accordingly, a Notice of Allowance is believed in order and is respectfully requested.

If the Examiner notes any further matters that the Examiner believes may be expedited by a telephone interview, the Examiner is requested to contact the undersigned at (650) 843-5608.

Respectfully submitted,

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